SUPPORT FOR THE AMENDMENTS

The present preliminary amendment amends the specification to include a section heading and a recitation of a claim of priority to related patent applications.

The present preliminary amendment cancels claims 1-4 and adds new claims 5-53.

Support for newly added claims 5, 21, 32 and 43 is found at specification page 3, lines 11-22, page 4, lines 1-5, page 7, lines 7-14, as well as claims 1 and 2.

Support for newly added claim 6-10 is found at specification page 4, line 1, page 6, lines 13-25, page 7, lines 7-14, as well as claim 2.

Support for newly added claims 11-13, 22-24, 33-35 and 44-46 is found at specification page 9, lines 18-27, and page 10, lines 1-12.

Support for newly added claims 14-18, 25-29, 36-40 and 47-51 is found at specification page 10, lines 14-24.

Support for newly added claims 19, 20, 30, 31, 41, 42, 52 and 53 is found at specification page 11, lines 8-14, page 15, lines 1-27, page 16, lines 1-27, and page 17, lines 1-20.

It is believed that the amendment to the specification and the addition of new claims 5-53 has not resulted in the introduction of new matter.

REMARKS

Claims 1-4 have been cancelled. Claims 5-53 have been added and are therefore currently pending in the present application

The rejection of claims 1-4 under 35 U.S.C. § 103(a) over either Izumi et al, Shin et al, Hirohiko et al, *or* Sarkar et al, in view of Endo et al is respectfully traversed.

Izumi et al is apparently relied upon by the Examiner for the disclosure of an anticancer medicine comprising a cholestanyl glycoside having a Fuc-Gal- sugar moiety. Applicants submit however that Izumi et al fails to disclose or suggest incorporating said cholestanyl Fuc-Gal- glycoside into a liposomal composition, which further comprises a phospholipid and a positive-charge-providing substance, as presently claimed.

Shin et al is apparently relied upon by the Examiner for the disclosure of an anticancer agent comprising a cholestanyl glycoside having a sugar moiety selected from the group consisting of GlcNAc-Gal-, Gal-Glc-, and Gal-. Applicants submit however that Shin et al fails to disclose or suggest incorporating said cholestanyl glycoside, having a sugar moiety selected from the group consisting of GlcNAc-Gal-, Gal-Glc-, and Gal-, into a liposomal composition, which further comprises a phospholipid and a positive-charge-providing substance, as presently claimed.

Hirohiko et al is apparently relied upon by the Examiner for the disclosure of a carcinostatic agent comprising an amino containing glycoside. Applicants submit however that there are a number of important distinctions between the amino containing glycoside of Hirohiko et al and the presently claimed amide containing glycoside according to formula (3). First, the glycoside of Hirohiko et al only has an amino substituent, whereas the presently claimed glycoside of formula (3) contains an amide substituent. In addition, Hirohiko et al fails to disclose or suggest a glycoside comprising the presently claimed sugar moietys.

Furthermore, the amino glycoside of Hirohiko et al only possesses a single carbon chain having from 16 to 20 carbon atoms. This hydrocarbon chain is much shorter in length than that of the presently claimed amide glycoside of formula (3), which possess not one, but two, carbon chains having from 15 to 29 carbon atoms, and from 18 to 32 carbon atoms, respectively. As a result, the presently claimed amide glycoside is therefore distinguished from the amino glycoside of Hirohiko et al, in that the amide glycoside of the present invention exhibits a much greater degree of hydrophobicity. Notwithstanding the aforementioned fundamental distinctions, Applicants submit that Hirohiko et al nevertheless fails to disclose or suggest incorporating said amino containing glycoside into a liposomal composition, which further comprises a phospholipid and a positive-charge-providing substance, as presently claimed.

Sarkar et al is apparently relied upon by the Examiner for the disclosure of a naphthalenyl glycoside having an GlcNAc-Gal- sugar moiety. Applicants submit however that unlike Sarkar et al, which discloses utilizing a naphthalenyl glycoside having a GlcNAc-Gal- sugar moiety as an anti-inflammatory agent, the present invention is drawn to utilizing the presently claimed naphthalenyl glycoside having a GlcNAc-Gal- sugar moiety according to formula (2) as an antitumor or anticancer agent. Applicants also submit that Sarkar et al fails to disclose or suggest incorporating said GlcNAc-Gal- containing naphthalenyl glycoside into a liposomal composition, which further comprises a phospholipid and a positive-charge-providing substance, as presently claimed.

As expressly acknowledged by the Examiner on page 3, lines 7 and 8, of the outstanding Official Action, each and every cited primary prior art reference is completely silent with respect to the critical limitation of incorporating the aforementioned glycosides into a liposomal composition that further comprises a phospholipid and a positive-charge-

providing substance, as presently claimed. The Examiner apparently attempts to compensate for this significant deficiency by relying on the disclosure of Endo et al.

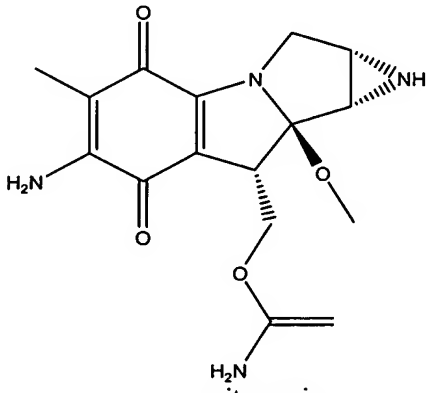
Applicants submit however that neither would it have been obvious to, nor would there have been sufficient motivation for, a skilled artisan to incorporate the presently claimed glycosides as active agents into the liposomal composition of Endo et al. For example, the cholestanyl glycosides of the present invention have chemical structures that are analogous to cholesterol. Cholesterol is well known as a vital constituent of plasma membranes, which surround the cells of all vertebrates. As a result, a skilled artisan would reasonably expect that the cholestanyl glycosides of the present invention would intrinsically possess sufficient affinity to cellular membranes without the aid of a liposomal carrier. Thus, it would not have been obvious, nor would there have been sufficient motivation, to incorporate the cholestanyl glycoside anticancer agents of the present invention into a liposomal carrier because a skilled artisan would not have reasonably expected that by doing so, one would impart any additional effects or benefits thereto.

Surprisingly however, the inventors have unexpectedly discovered that by incorporating the cholestanyl glycoside anticancer agents into the liposomal carrier, the liposomal composition of the present invention exhibited greatly enhanced antitumor efficacy far beyond that achieved by the sole administration of the cholestanyl glycoside anticancer agents alone. These unexpected and unforeseeable results are illustrated in the originally filed specification in Figures 1 and 2, which demonstrate by means of comparative experimental evidence, the unpredictable and excellent effects achieved by administering the presently claimed liposomal composition comprising the cholestanyl glycoside anticancer agents incorporated within the liposomal carrier.

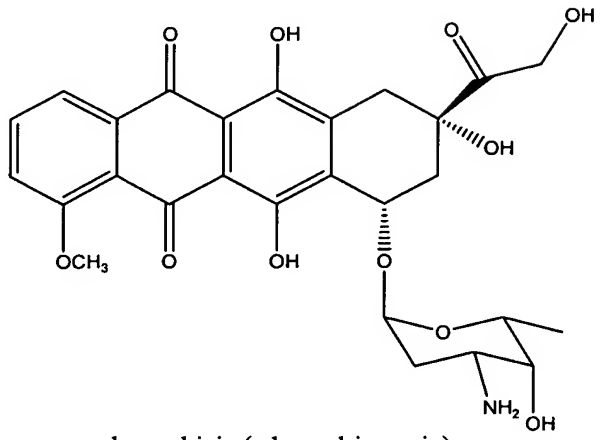
Applicants further submit that while Endo et al discloses incorporating a carcinostatic active agent into a liposomal composition comprising a phospholipid (e.g., a phospholipid

such as dipalmitoylphosphatidylcholine) and a positive-charge-providing substance (e.g., an aliphatic amine such as stearylamine), said carcinostatic agent is present in a laundry list of more than twenty widely diversified types of active agents. Applicants submit that there is a complete lack of motivation to pick and chose carcinostatic agents therefrom. Assuming *arguendo* that there was in fact a sufficient motivation for selecting carcinostatic agents from the list of over twenty types of active agents, Applicants submit that it would certainly not have been obvious to a skilled artisan to select a glycoside as said carcinostatic agent from the thousands, if not hundreds of thousands, of carcinostatic agents known in the art at the time the instant application was filed. Moreover, absent impermissible hindsight reconstruction, a skilled artisan would not have had sufficient motivation, much less a reasonable expectation of success, in substituting a glycoside for any one of the carcinostatic agents defined in Endo et al. This is particularly evidenced by the fact that the antitumor antibiotics (i.e., mitomycin, doxorubicin or adriamycin), antimetabolites (i.e., methotrexate and tegafur), platinum compound (i.e., cisplatin), and vinca alkaloid (i.e., vincristine) carcinostatic agents explicitly set forth in Endo et al (column 4, lines 51 and 52) are vastly different in chemical structure in comparison to those of instantly claimed glycosides, as shown in greater detail hereinbelow:

• Antitumor Antibiotic Carcinostatic Agents (i.e., mitomycin, doxorubicin or adriamycin)

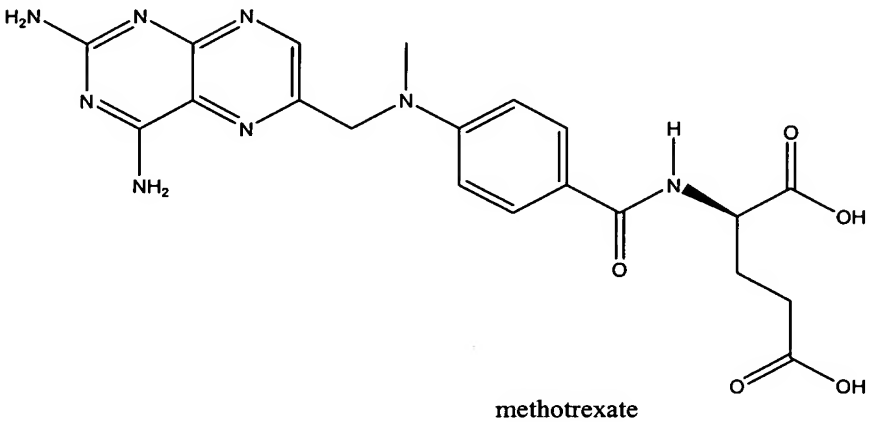


mitomycin

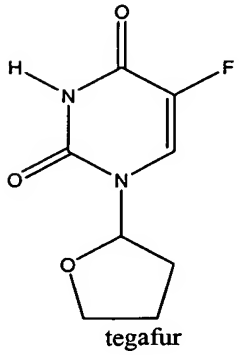


doxorubicin (a.k.a. adriamycin)

• Antimetabolite Carcinostatic Agents (i.e., methotrexate and tegafur)

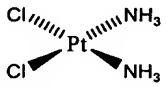


methotrexate



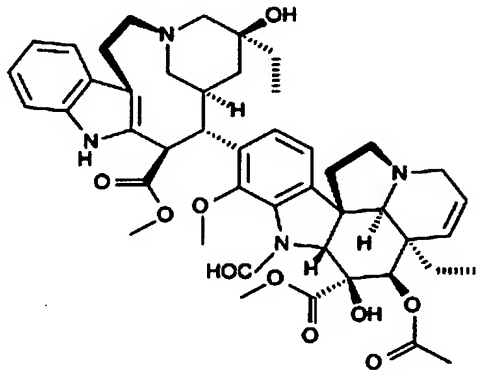
tegafur

• Platinum Compound Carcinostatic Agent (i.e., cisplatin)



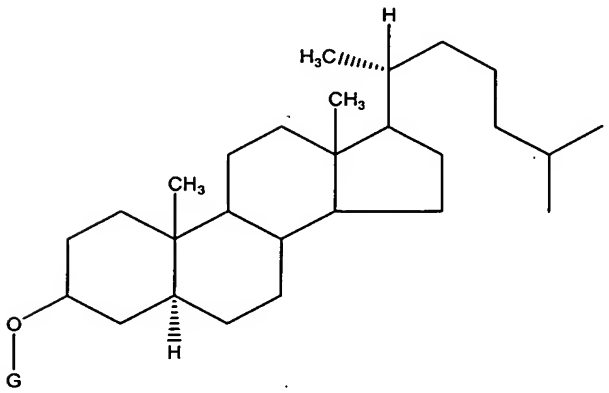
cisplatin

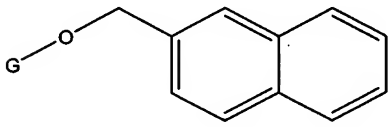
• Vinca Alkaloid Carcinostatic Agent (i.e., vincristine)

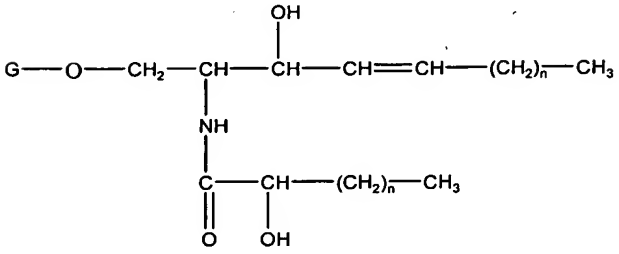


vincristine

In sharp contrast to the previously illustrated carcinostatic agents disclosed in Endo et al, the glycosides of the present invention are dramatically different in chemical structure, as demonstrated hereinbelow:







In conclusion, absent impermissible hindsight reconstruction, a skilled artisan would not have had sufficient motivation, much less a reasonable expectation of success, in substituting the presently claimed glycosides for any one of the carcinostatic agents disclosed in Endo et al.

In view of the foregoing, withdrawal of this ground of rejection is respectfully requested.

The objection to the specification for failing to include a cross-reference to related applications is obviated by the foregoing amendment to the specification, which now recites a claim for international and foreign priority.

In view of the foregoing, withdrawal of this objection is respectfully requested.

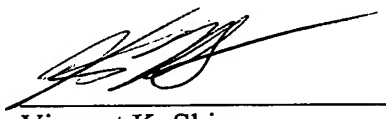
The objection to claim 4 as being an improper multiple dependent claim is obviated by the foregoing amendment canceling said claim.

In view of the foregoing, withdrawal of this objection is respectfully requested.

Applicants submit that the present application is in condition for allowance and notification to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



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